

DAIDS Bethesda, MD USA	<b>POLICY</b>	No.: DWD-POL-SR-02.00
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	Approval Date: 20 DEC 06 Effective Date: 05 FEB 07	Replaces: V 1.0

## 1.0 PURPOSE

This policy is designed to ensure consistent and acceptable standards of expedited adverse event reporting to the Division of Acquired Immunodeficiency Syndrome (DAIDS) by investigators participating in DAIDS funded and/or sponsored clinical trials.

## 2.0 SCOPE

This policy applies to all DAIDS funded and/or sponsored clinical trials.

## 3.0 BACKGROUND

In the past, DAIDS has used several different serious adverse event (SAE) reporting manuals, reporting forms, and severity grading tables, depending on the type of study conducted. With the expansion of DAIDS international research, as well as the coordination of treatment, prevention, and vaccine research, the need to develop DAIDS-wide policies and procedures for expedited reporting of adverse events has been recognized and addressed. This policy is in accordance with the US Code of Federal Regulations, the Office for Human Research Protections (CFR and OHRP), International Conference on Harmonisation (ICH) guidelines, National Institutes of Health (NIH) policy, and the National Institute of Allergy and Infectious Diseases (NIAID) Clinical Terms of Awards.

## 4.0 DEFINITIONS

**Adverse Event (AE)** – Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. In addition, if an untoward medical occurrence occurs as a result of study participation or study-related interventions, it is considered to be an adverse event.

**Serious Adverse Event (SAE)** – Any untoward medical occurrence that, at any dose, results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. This includes important medical events that may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the patient or may require intervention to prevent one of the outcomes listed in the definition above.

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**Expedited Adverse Event (EAE)** – An adverse event that meets the criteria for expedited reporting, as specified in the Manual for Expedited Reporting of Adverse Events to DAIDS.

**Division of AIDS Safety Office** – The Office to which adverse events requiring expedited reporting are submitted. Currently located in the Regulatory Affairs Branch (RAB), Office for Policy in Clinical Research Operations (OPCRO) support contract and managed through RAB.

**Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (Toxicity Table)** – A list of common terms and severity (intensity) parameters used to describe adverse events occurring in DAIDS funded and/or sponsored clinical studies/trials.

**Investigator of Record (IoR)** – The person responsible for the conduct of the clinical trial at a clinical research site. This person is the signatory for the Form FDA 1572 (IND studies) or the DAIDS IoR Agreement (non-IND studies).

**Principal Investigator (PI)** – A qualified person designated by the applicant institution to direct the research. PIs oversee the scientific and technical aspects of a grant and the day-to-day management of the research.

For additional definitions, see DAIDS glossary.

## 5.0 RESPONSIBILITIES

In accordance with the U.S. Code of Federal Regulations and ICH guidelines, as the sponsor of a clinical trial, DAIDS is responsible for prompt and accurate reporting to the FDA of any serious and unexpected (i.e., not listed in the investigator's brochure or package insert) adverse events associated with the use of a study agent. All investigators using the study agent in DAIDS funded and/or sponsored human subjects clinical trials must also receive copies of the reports submitted to the FDA for submission to the IRB/EC.

The Investigator of Record conducting DAIDS clinical trial is responsible for reporting all EAEs occurring at the clinical research site to the DAIDS Safety Office as soon as possible, and according to timeframes identified in the Manual for Expedited Reporting of Adverse Events to DAIDS.

The Principal Investigator (PI) is responsible for submitting all the necessary documents and reports to the host country regulatory authorities for studies conducted outside of the United States. Documentation of all correspondence and

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approval from the host country regulatory authorities must be provided to the appropriate DAIDS program staff prior to study initiation in the host country.

## 6.0 POLICY

- 6.1. All DAIDS funded and/or sponsored clinical trials must use the current Manual for Expedited Reporting of Adverse Events to DAIDS (EAE Reporting Manual), DAIDS Expedited Adverse Event Form (EAE Form), and the DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (AE Grading Table) when reporting adverse events on an expedited basis. All adverse events that meet the criteria for expedited reporting to DAIDS must be submitted to DAIDS Safety Office in English within the time period specified in the EAE Reporting Manual. However, ongoing studies supported or funded by DAIDS may continue use of legacy reporting systems until further notification by OPCRO.
- 6.2. The study protocol must specify which level of expedited adverse event reporting will be used, the study agents that will be considered in determining the relationship to any adverse events that occur, the AE grading table which will be used to determine the severity of adverse events, and the duration of the EAE reporting period. Additional adverse event reporting requirements may be added to the protocol on a case-by-case basis.
- 6.3. DAIDS will maintain a distribution plan and tracking method for sending IND Safety Reports and MedWatch reports to DAIDS investigators, other collaborators and pharmaceutical sponsors.
- 6.4. Any modification to these requirements must be approved in writing by the OPCRO Director or designee. Documentation of OPCRO approval will be available to DAIDS staff.

## 7.0 REFERENCES

International Conference on Harmonisation Guidance for Industry, Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (E2A)  
<http://www.ich.org/LOB/media/MEDIA-436.pdf>

International Conference on Harmonisation Guidance for Industry, Good Clinical Practice: Consolidated Guideline (E6)  
<http://www.fda.gov/oc/gcp/guidance.html>

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U.S. Code of Federal Regulations, Title 21, Part 312

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>

NIAID Clinical Terms of Award

<http://www.niaid.nih.gov/ncn/pdf/clinterm.pdf>

DAIDS Expedited Adverse Event Reporting Materials (EAE Reporting Manual, Forms, AE Grading Table, guidance, and template protocol language).

<http://rcc.tech-res.com/eae.htm>

## 8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at: [NIAIDOPCROPOLICYGROUP@mail.nih.gov](mailto:NIAIDOPCROPOLICYGROUP@mail.nih.gov)

## 9.0 AVAILABILITY

This policy is available electronically at the following URL:

<http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm>

The signed original is maintained in the OPCRO policy office.

## 10.0 CHANGE SUMMARY

Version #	Date	Replaces	Date of Revision	Rationale for Revision/Retirement
2.0	20 DEC 06	V 1.0	20 DEC 06	DAIDS Final Review
1.0	14 JUL 06	N/A	N/A	N/A

## 11.0 APPENDICES

The following materials are available for download at the DAIDS Safety Office website: <http://rcc.tech-res.com/eae.htm>

- Manual for Expedited Reporting of Adverse Events to DAIDS
- DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events
- DAIDS Safety Office Expedited Adverse Event (EAE) Form

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- Completion Instructions for the DAIDS EAE Form
- Template Wording for the Expedited Adverse Event Reporting Section of DAIDS-Sponsored Protocols

## 12.0 APPROVAL

Signature	Program/Branch	Date
Authorized By: <u><i>Richard Hafner</i></u> Richard Hafner, MD Director	Office for Policy in Clinical Research Operations (OPCRO)	<u>December 20, 2006</u>